REMARKS

Claim Amendments

Claims 1-3, 5-14 and 16-17 have been amended, claim 4 has been cancelled, without prejudice, and replaced with new claim 18; and claim 15 has been cancelled and replaced with new claim 19. Following entry of these amendments, claims 1-3, 5-14 and 16-17 are pending in this application.

More specifically, claims 1, 2, 3 and 13 have been converted from "use" form to an appropriate method of use form, consistent with the method of original claim 17. Compound claim 4 has been cancelled and rewritten as self-contained compound claim 18, directly incorporating the appropriate compound formula (II) and the moiety definitions, which were indirectly incorporated by reference to claim 1 in original claim 4. Claims 1-12 have been amended to change their dependency from original claim 1 to replacement independent compound claim 18. Claims 14 and 16-17 have been amended to update their dependencies to refer to claims 18 and 5-12. Process for making claim 15 (originally dependent on "use" claim 1) has been rewritten as new claim 19, which is more appropriately dependent on the compound definition of claim 18 and related compound formula (II).

Support for all of these amendments is found in the original claims as filed, as well as throughout the specification, and no new matter has been added. Accordingly, entry of these amendments is believed to be in order, and entry of the same is respectfully requested.

Specification Amendment

An Abstract has been provided, typed on a separate page as requested by the Examiner. However, it should be recognized that this is a duplicate of the Abstract properly filed in the international application, and included with this application as filed. The purpose of the request for this duplicate Abstract is therefore not understood. The Examiner's attention is respectfully called to MPEP ¶1893.03(e), which provides in part:

> Since applicant has already complied with PCT Rule 11.4 by filing the abstract on a separate sheet when the international application was filed, it is improper for the examiner of the U.S. national stage application to require an abstract on a separate sheet during national stage processing of the international application.

Claim Rejections – 35 USC § 112

Claims 1-3 and 13 have been rejected as being in an improper "use" format. These claims have been converted by the above amendments to a method of treatment format. Therefore, this ground for rejection has been overcome.

Claim 15 has been rejected as reciting "the limitation 'R^{62}' in formula I" on the ground that there is insufficient antecedent basis of this limitation in the claim. The basis for this rejection is not understood. In any event, claim 15 has been cancelled and replaced with new process claim 19. In process claim 19, subparagraph (d), R^2 is defined as R^5X^1, wherein X^1 is as defined in claim 18, and R^5 is $C_{1\text{-}5}$alkylR^{62}, wherein R^{62} is selected from one of the nine groups that follow in claim 19. The group R^{62} is again used in formula (X) of claim 19, wherein R^{62} is "as defined herein". Therefore, proper antecedent basis for the group R^{62}

appears throughout claim 19, and any basis there may have been for this rejection of claim 15 is not present in new claim 19.

Claim Objections

All objections with respect to improper multiple dependencies are believed to have been overcome by the above amendments to the claims.

Claim Rejections – 35 USC § 102

Claims 1 and 17 have been rejected under section 102(b) as being inherently anticipated by the Myers *et al.* reference. This ground for rejection is respectfully traversed, in view of the above claim amendments converting the "use" claims into an appropriate method of treatment form, and the following remarks. In particular, Myers *et al.* does not teach the method of treatment as presently claimed.

Myers *et al.* is not directed towards antiangiogenic agents, nor does it describe inhibitors of vascular endothelial growth factor (VEGF) receptor tyrosine kinase (RTK). Instead Myers *et al.*, page 3, lines 26-27, is directed to the inhibition of "CSF-1 and CSF-2 receptor signaling in bone remodeling and haematopoeisis". Myers *et al.*, page 3, lines 11-13, describes compounds which are "inhibitors of colony stimulating factor-1 receptor tyrosine kinase, CSF-1R, activity and have activity in a $p56^{lck}$ cell-free assay." The compounds page 3, lines 15-16, "do not demonstrate significant PDGF-R activity in a cell-free assay" and, page 3, lines 23-24, "CSF-1R and PDGF-R (platelet derived growth factor receptor) are closely related." Furthermore the reference states at page 3, lines 25-26,

"compounds of this invention are selective inhibitors of CSF-1R tyrosine kinase activity" (emphasis added). It is suggested in Myers et al, page 3, lines 16-19, that the compounds therein may inhibit other src-like tyrosine kinases involved in the signal transduction pathway. However, it should be noted that VEGF RTK is not a src-like tyrosine kinase. VEGF RTK is a transmembrane RTK, unlike src which is an intracellular RTK. This means that VEGF RTK is a receptor tyrosine kinase and src is a non-receptor tyrosine kinase. VEGF RTK and src are in different families or RTK. The compounds of Myers *et al.* are said to be useful for the inhibition of cell proliferation and/or differentiation and/or mediator release by effectively inhibiting CSF-1R activity - see claim 1. Nowhere in Myers et al is there any mention of VEGF, its receptors, angiogenesis or vascular permeability.

Therefore, the method of treatment claimed in claims 1 and 17 of the present application is novel, and is not defined in Myers *et al.* Accordingly, this ground for rejection should be withdrawn.

Information Disclosure Statement

The Examiner's attention is respectfully drawn to the Information Disclosure Statement filed herewith.

Conclusion

In view of the above amendments and the foregoing remarks, it is believed that all claims are in appropriate form and patentable over the record art. Accordingly, withdrawal of all grounds for rejection and the allowance of all claims are believed to be in order, and are respectfully requested.

Respectfully Submitted,
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Date: November 6, 2002 By: _____

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APPENDIX
VERSION WITH MARKINGS TO SHOW CHANGES

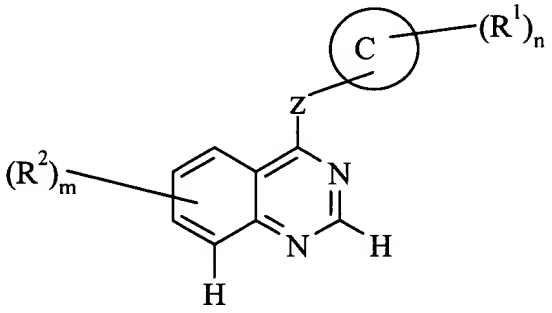
IN THE ABSTRACT:

A duplicate abstract has been presented on a separate page (per the Examiner's specific request), which is the same as the official abstract that was properly filed in the International Application and submitted with this application as filed.

IN THE CLAIMS:

Claims 1-3, 6-14 and 16-17 have been amended as follows, wherein added material is shown by **bold underlined text**, and deleted material is shown by **[bold text in brackets]**:

1. (Amended) **[The use]** **A method for producing an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal in need thereof, which comprises administering to said animal an effective amount** of a compound of the formula I:



(I)

wherein:

ring C is a 5-6-membered heterocyclic moiety which may be saturated or unsaturated, which may be aromatic or non-aromatic, and which contains 1-3 heteroatoms selected independently from O, N and S;

Z is -O-, -NH-, -S- or -CH_2-;

R^1 represents hydrogen, C_{1-4}alkyl, C_{1-4}alkoxymethyl, di(C_{1-4}alkoxy)methyl, C_{1-4}alkanoyl, trifluoromethyl, cyano, amino, C_{2-5}alkenyl, C_{2-5}alkynyl, a phenyl group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be aromatic or non-aromatic and may be saturated (linked via a ring carbon or nitrogen atom) or unsaturated (linked via a ring carbon atom), and which phenyl, benzyl or heterocyclic group may bear on one or more ring carbon atoms up to 5 substituents selected from hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C_{2-4}alkanoyl, C_{1-4}alkanoylamino, C_{1-4}alkoxycarbonyl, C_{1-4}alkylsulphanyl, C_{1-4}alkylsulphinyl, C_{1-4}alkylsulphonyl, carbamoyl, N-C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, aminosulphonyl, N-C_{1-4}alkylaminosulphonyl, N,N-di(C_{1-4}alkyl)aminosulphonyl, C_{1-4}alkylsulphonylamino, C_{1-4}alkylamino, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}haloalkyl, C_{1-4}hydroxyalkoxy, carboxy and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C_{1-4}alkoxycarbonyl; and additionally R^1 may represent carboxy, C_{3-7}cycloalkyl, C_{3-7}cycloalkylC_{1-3}alkyl, or phenylC_{2-4}alkyl wherein the phenyl moiety may bear up to 5 substituents selected from the list herein defined for a phenyl ring which is directly linked to ring C;

n is an integer from 0 to 5;

m is an integer from 0 to 3;

R^2 represents hydrogen, hydroxy, halogeno, cyano, nitro, trifluoromethyl, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkylsulphanyl, -NR^3R^4 (wherein R^3 and R^4, which may be the same or different, each represents hydrogen or C_{1-3}alkyl), or R^5X^1- (wherein X^1 represents a direct

bond, -O-, -CH_2-, -OCO-, carbonyl, -S-, -SO-, -SO_2-, -NR^6CO-, -$CONR^7$-, -SO_2NR^8-, -NR^9SO_2- or -NR^{10}- (wherein R^6, R^7, R^8, R^9 and R^{10} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl), and R^5 is selected from one of the following eighteen groups:

1) hydrogen or C_{1-5}alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro, chloro, bromo and amino;
2) C_{1-5}alkylX^2COR^{11} (wherein X^2 represents -O- or -NR^{12}- (in which R^{12} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{11} represents C_{1-3}alkyl, -$NR^{13}R^{14}$ or -OR^{15} (wherein R^{13}, R^{14} and R^{15} which may be the same or different each represents hydrogen, C_{1-3}alkyl, C_{4-5}alkyl or C_{1-3}alkoxyC_{2-3}alkyl));
3) C_{1-5}alkylX^3R^{16} (wherein X^3 represents -O-, -S-, -SO-, -SO_2-, -OCO-, -$NR^{17}CO$-, -$CONR^{18}$-, -SO_2NR^{19}-, -$NR^{20}SO_2$- or -NR^{21}- (wherein R^{17}, R^{18}, R^{19}, R^{20} and R^{21} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{16} represents hydrogen, C_{1-3}alkyl, cyclopentyl, cyclohexyl or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C_{1-3}alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C_{1-4}alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}cyanoalkyl and C_{1-4}alkoxycarbonyl);
4) C_{1-5}alkylX^4C_{1-5}alkylX^5R^{22} (wherein X^4 and X^5 which may be the same or different are each -O-, -S-, -SO-, -SO_2-, -$NR^{23}CO$-, -$CONR^{24}$-, -SO_2NR^{25}-, -$NR^{26}SO_2$- or -NR^{27}- (wherein R^{23}, R^{24}, R^{25}, R^{26} and R^{27} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{22} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl);
5) R^{28} (wherein R^{28} is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}alkoxyC_{1-4}alkyl, C_{1-4}alkylsulphonylC_{1-4}alkyl and C_{1-4}alkoxycarbonyl);

6) C_{1-5}alkylR^{28} (wherein R^{28} is as defined herein);

7) C_{2-5}alkenylR^{28} (wherein R^{28} is as defined herein);

8) C_{2-5}alkynylR^{28} (wherein R^{28} is as defined herein);

9) R^{29} (wherein R^{29} represents a pyridone group, a phenyl group or a 5-6-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-3 heteroatoms selected from O, N and S, which pyridone, phenyl or aromatic heterocyclic group may carry up to 5 substituents on an available carbon atom selected from hydroxy, halogeno, amino, C_{1-4}alkyl, C_{1-4}alkoxy, C_{1-4}hydroxyalkyl, C_{1-4}aminoalkyl, C_{1-4}alkylamino, C_{1-4}hydroxyalkoxy, carboxy, trifluoromethyl, cyano, $-CONR^{30}R^{31}$ and $-NR^{32}COR^{33}$ (wherein R^{30}, R^{31}, R^{32} and R^{33}, which may be the same or different, each represents hydrogen, C_{1-4}alkyl or C_{1-3}alkoxyC_{2-3}alkyl));

10) C_{1-5}alkylR^{29} (wherein R^{29} is as defined herein);

11) C_{2-5}alkenylR^{29} (wherein R^{29} is as defined herein);

12) C_{2-5}alkynylR^{29} (wherein R^{29} is as defined herein);

13) C_{1-5}alkylX^6R^{29} (wherein X^6 represents -O-, -S-, -SO-, $-SO_2-$, $-NR^{34}CO-$, $-CONR^{35}-$, $-SO_2NR^{36}-$, $-NR^{37}SO_2-$ or $-NR^{38}-$ (wherein R^{34}, R^{35}, R^{36}, R^{37} and R^{38} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{29} is as defined herein);

14) C_{2-5}alkenylX^7R^{29} (wherein X^7 represents -O-, -S-, -SO-, $-SO_2-$, $-NR^{39}CO-$, $-CONR^{40}-$, $-SO_2NR^{41}-$, $-NR^{42}SO_2-$ or $-NR^{43}-$ (wherein R^{39}, R^{40}, R^{41}, R^{42} and R^{43} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{29} is as defined herein);

15) C_{2-5}alkynylX^8R^{29} (wherein X^8 represents -O-, -S-, -SO-, $-SO_2-$, $-NR^{44}CO-$, $-CONR^{45}-$, $-SO_2NR^{46}-$, $-NR^{47}SO_2-$ or $-NR^{48}-$ (wherein R^{44}, R^{45}, R^{46}, R^{47} and R^{48} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{29} is as defined herein);

16) C_{1-3}alkylX^9C_{1-3}alkylR^{29} (wherein X^9 represents -O-, -S-, -SO-, $-SO_2-$, $-NR^{49}CO-$, $-CONR^{50}-$, $-SO_2NR^{51}-$, $-NR^{52}SO_2-$ or $-NR^{53}-$ (wherein R^{49}, R^{50}, R^{51}, R^{52} and R^{53} each

independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{29} is as defined herein);

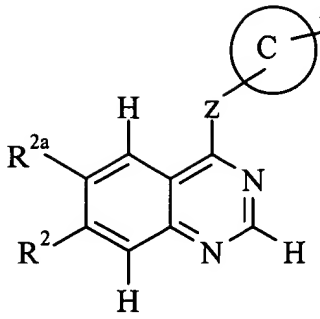
17) C_{1-3}alkylX^9C_{1-3}alkylR^{28} (wherein X^9 and R^{28} are as defined herein); and

18) C_{1-3}alkyl$R^{54}C_{1-3}$alkylX^9R^{55} (wherein X^9 is as defined herein and R^{54} and R^{55} are each independently selected from hydrogen, C_{1-3}alkyl, cyclopentyl, cyclohexyl and a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C_{1-3}alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C_{1-4}alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, C_{1-4}cyanoalkyl and C_{1-4}alkoxycarbonyl), with the proviso that R^{54} cannot be hydrogen;

and additionally wherein any C_{1-5}alkyl, C_{2-5}alkenyl or C_{2-5}alkynyl group in R^5X^1- may bear one or more substituents selected from hydroxy, halogeno and amino;

or a **pharmaceutically acceptable** salt thereof **[in the manufacture of a medicament for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals such as humans]**.

2. (Amended) [The use] **A method for producing an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal in need thereof, which comprises administering to said animal an effective amount** of a compound of the formula Ia:



(Ia)

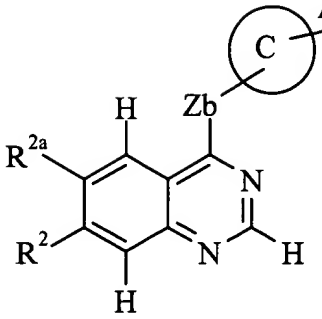
wherein:

ring C, R^1, R^2, n and Z are as defined in claim 1 with the proviso that R^2 is not hydrogen; and

R^{2a} represents hydrogen, halogeno, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkylthio, $-NR^{3a}R^{4a}$ (wherein R^{3a} and R^{4a}, which may be the same or different, each represents hydrogen or C_{1-3}alkyl), or $R^{5a}(CH_2)_{za}X^{1a}$ (wherein R^{5a} is a 5- or 6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl and C_{1-4}alkoxy, za is an integer from 0 to 4 and X^{1a} represents a direct bond, -O-, $-CH_2-$, -S-, -SO-, $-SO_2-$, $-NR^{6a}CO-$, $-CONR^{7a}-$, $-SO_2NR^{8a}-$, $-NR^{9a}SO_2-$ or $-NR^{10a}-$ (wherein R^{6a}, R^{7a}, R^{8a}, R^{9a} and R^{10a} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl));

or a **pharmaceutically acceptable** salt thereof**], in the manufacture of a medicament for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals such as humans]**.

3. (Amended) **[The use]** **A method for producing an antiangiogenic or vascular permeability reducing effect in a warm-blooded animal in need thereof, which comprises administering to said animal an affective amount** of a compound of the formula Ib:



(Ib)

wherein:

ring C, R^1, R^2 and n are as defined in claim 1 with the proviso that R^2 is not hydrogen, R^{2a} is as defined in claim 2; and

Zb is -O- or -S-;

or a **pharmaceutically acceptable** salt thereof**[, in the manufacture of a medicament for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals such as humans]**.

5. (Amended) A compound as claimed in claim **18 [4]** wherein Zb is -O-.

6. (Amended) A compound as claimed in claim **18 [4 or claim 5]** wherein R^{2a} is methoxy.

7. (Amended) A compound as claimed in **claim 18 [any one of claims 4-6]** wherein ring C is a 5-membered heteroaromatic moiety which contains 1-3 heteroatoms selected independently from O, N and S.

8. (Amended) A compound as claimed in **claim 18 [any one of claims 4-7]** wherein R^1 is a phenyl group or a 5-6-membered heteroaromatic group with 1-3 heteroatoms, selected independently from O, S and N, (linked via a ring carbon atom), which phenyl or heteroaromatic group is optionally substituted as defined in claim **18 [1]**.

9. (Amended) A compound as claimed in **claim 18 [any one of claims 4-8]** wherein

R^2 represents hydroxy, halogeno, nitro, trifluoromethyl, C_{1-3}alkyl, cyano, amino or R^5X^1-[]wherein X^1 is as defined in claim **18** **[1]** and R^5 is selected from one of the following eighteen groups:

1) C_{1-4}alkyl which may be unsubstituted or substituted with one or more fluorine atoms, or C_{2-4}alkyl which may be unsubstituted or substituted with 1 or 2 groups selected from hydroxy and amino;
2) C_{2-3}alkylX^2COR^{11} (wherein X^2 is as defined in claim **18** **[1]** and R^{11} represents -$NR^{13}R^{14}$ or -OR^{15} (wherein R^{13}, R^{14} and R^{15} which may be the same or different are each C_{1-2}alkyl or C_{1-2}alkoxyethyl));
3) C_{2-4}alkylX^3R^{16} (wherein X^3 is as defined in claim **18** **[1]** and R^{16} is a group selected from C_{1-3}alkyl, cyclopentyl, cyclohexyl, pyrrolidinyl and piperidinyl which group is linked to X^3 through a carbon atom and which C_{1-3}alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C_{1-2}alkoxy and which cyclopentyl, cyclohexyl, pyrrolidinyl or piperidinyl group may carry one substituent selected from oxo, hydroxy, halogeno, C_{1-2}alkyl, C_{1-2}hydroxyalkyl and C_{1-2}alkoxy);
4) C_{2-3}alkylX^4C_{2-3}alkylX^5R^{22} (wherein X^4 and X^5 are as defined in claim **18** **[1]** and R^{22} represents hydrogen or C_{1-3}alkyl);
5) C_{1-4}alkylR^{59} (wherein R^{59} is a group selected from pyrrolidinyl, piperazinyl, piperidinyl, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithiolan-2-yl and 1,3-dithian-2-yl, which group is linked to C_{1-4}alkyl through a carbon atom and which group may carry 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-2}alkoxyC_{1-3}alkyl and C_{1-2}alkylsulphonylC_{1-3}alkyl) or C_{2-4}alkylR^{60} (wherein R^{60} is a group selected from morpholino, thiomorpholino, pyrrolidin-1-yl, piperazin-1-yl and piperidino which group may carry 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}hydroxyalkyl, C_{1-3}alkoxy, C_{1-2}alkoxyC_{1-3}alkyl and C_{1-2}alkylsulphonylC_{1-3}alkyl);
6) C_{3-4}alkenylR^{61} (wherein R^{61} represents R^{59} or R^{60} as defined herein);
7) C_{3-4}alkynylR^{61} (wherein R^{61} represents R^{59} or R^{60} as defined herein);
8) R^{29} (wherein R^{29} is as defined in claim **18** **[1]**);

9) C_{1-4}alkylR^{29} (wherein R^{29} is as defined in claim **18** [1]);

10) 1-R^{29}prop-1-en-3-yl or 1-R^{29}but-2-en-4-yl (wherein R^{29} is as defined in claim **18** [1] with the proviso that when R^5 is 1-R^{29}prop-1-en-3-yl, R^{29} is linked to the alkenyl group via a carbon atom);

11) 1-R^{29}prop-1-yn-3-yl or 1-R^{29}but-2-yn-4-yl (wherein R^{29} is as defined in claim **18** [1] with the proviso that when R^5 is 1-R^{29}prop-1-yn-3-yl, R^{29} is linked to the alkynyl group via a carbon atom);

12) C_{1-5}alkylX^6R^{29} (wherein X^6 and R^{29} are as defined in claim **18** [1]);

13) 1-($R^{29}X^7$)but-2-en-4-yl (wherein X^7 and R^{29} are as defined in claim **18** [1]);

14) 1-($R^{29}X^8$)but-2-yn-4-yl (wherein X^8 and R^{29} are as defined in claim **18** [1]);

15) C_{2-3}alkylX^9C_{1-2}alkylR^{29} (wherein X^9 and R^{29} are as defined in claim **18** [1]);

16) R^{28} (wherein R^{28} is as defined in claim **18** [1]);

17) C_{2-3}alkylX^9C_{1-2}alkylR^{28} (wherein X^9 and R^{28} are as defined in claim **18** [1]); and

18) C_{2-3}alkyl$R^{54}C_{1-2}$alkylX^9R^{55} (wherein X^9, R^{54} and R^{55} are as defined in claim **18** [1]);

and additionally wherein any C_{1-5}alkyl, C_{2-5}alkenyl or C_{2-5}alkynyl group in R^5X^1- may bear one or more substituents selected from hydroxy, halogeno and amino**[]**.

10. (Amended) A compound as claimed in **claim 18 [any one of claims 4-9]** wherein R^2 represents 2-methoxyethoxy, 2-(2-methoxyethoxy)ethoxy, 3-methoxypropoxy, 2-methylsulphonylethoxy, 3-methylsulphonylpropoxy, 2-(tetrahydropyran-4-yloxy)ethoxy, 3-(tetrahydropyran-4-yloxy)propoxy, 2-(4-methylpiperazin-1-yl)ethoxy, 3-(4-methylpiperazin-1-yl)propoxy, 2-morpholinoethoxy, 3-morpholinopropoxy, 2-(imidazol-1-yl)ethoxy, 3-(imidazol-1-yl)propoxy 2-(1,1-dioxothiomorpholino)ethoxy, 3-(1,1-dioxothiomorpholino)propoxy, 2-(1,2,3-triazol-1-yl)ethoxy, 3-(1,2,3-triazol-1-yl)propoxy, 2-(N-methoxyacetyl-N-methylamino)ethoxy, 3-(N-methoxyacetyl-N-methylamino)propoxy, N-methylpiperidin-3-ylmethoxy, 4-(pyrrolidin-1-yl)but-2-en-yloxy, 2-(2-oxopyrrolidin-1-yl)ethoxy, 3-(2-oxopyrrolidin-1-yl)propoxy, 2-(pyrrolidin-1-yl)ethoxy, 3-(pyrrolidin-1-yl)propoxy, 2-(2-(pyrrolidin-1-yl)ethoxy)ethoxy, 2-(2-(4-methylpiperazin-1-yl)ethoxy)ethoxy,

2-piperidinoethoxy, 3-piperidinopropoxy, 2-(methylpiperidino)ethoxy,
3-(methylpiperidino)propoxy, 2-(ethylpiperidino)ethoxy, 3-(ethylpiperidino)propoxy,
2-((2-methoxyethyl)piperidino)ethoxy, 3-((2-methoxyethyl)piperidino)propoxy,
2-((2-methylsulphonyl)ethylpiperidino)ethoxy,
3-((2-methylsulphonyl)ethylpiperidino)propoxy, piperidin-3-ylmethoxy,
piperidin-4-ylmethoxy, 2-(piperidin-3-yl)ethoxy, 2-(piperidin-4-yl)ethoxy,
3-(piperidin-3-yl)propoxy, 3-(piperidin-4-yl)propoxy, 2-(methylpiperidin-3-yl)ethoxy,
2-(methylpiperidin-4-yl)ethoxy, 3-(methylpiperidin-3-yl)propoxy,
3-(methylpiperidin-4-yl)propoxy, 2-(ethylpiperidin-3-yl)ethoxy,
2-(ethylpiperidin-4-yl)ethoxy, 3-(ethylpiperidin-3-yl)propoxy,
3-(ethylpiperidin-4-yl)propoxy, 2-((2-methoxyethyl)piperidin-3-yl)ethoxy,
2-((2-methoxyethyl)piperidin-4-yl)ethoxy, 3-((2-methoxyethyl)piperidin-3-yl)propoxy,
3-((2-methoxyethyl)piperidin-4-yl)propoxy,
2-((2-methylsulphonylethyl)piperidin-3-yl)ethoxy,
2-((2-methylsulphonylethyl)piperidin-4-yl)ethoxy,
3-((2-methylsulphonylethyl)piperidin-3-yl)propoxy,
3-((2-methylsulphonylethyl)piperidin-4-yl)propoxy, 1-isopropylpiperidin-2-ylmethyl,
1-isopropylpiperidin-3-ylmethyl, 1-isopropylpiperidin-4-ylmethyl,
2-(1-isopropylpiperidin-2-yl)ethyl, 2-(1-isopropylpiperidin-3-yl)ethyl,
2-(1-isopropylpiperidin-4-yl)ethyl, 3-(1-isopropylpiperidin-2-yl)propyl,
3-(1-isopropylpiperidin-3-yl)propyl, 3-(1-isopropylpiperidin-4-yl)propyl,
3-(4-methylpiperazin-1-yl)propoxy, 1-methylpiperidin-4-ylmethoxy,
1-(2-methylsulphonylethyl)piperidin-4-ylmethoxy,
1-(2-pyrrolidinylethyl)piperidin-4-ylmethoxy,
1-(3-pyrrolidinylpropyl)piperidin-4-ylmethoxy, 1-(2-piperidinylethyl)piperidin-4-ylmethoxy,
1-(3-piperidinylpropyl)piperidin-4-ylmethoxy, 1-(2-morpholinoethyl)piperidin-4-ylmethoxy,
1-(3-morpholinopropyl)piperidin-4-ylmethoxy,
1-(2-thiomorpholinoethyl)piperidin-4-ylmethoxy,

1-(3-thiomorpholinopropyl)piperidin-4-ylmethoxy,
1-(2-azetidinylethyl)piperidin-4-ylmethoxy or 1-(3-azetidinylpropyl)piperidin-4-ylmethoxy.

11. (Amended) A compound as claimed in claim **18** **[4]** selected from:
4-(5-(4-methoxyphenyl)pyrazol-3-yloxy)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)-quinazoline,
4-(5-(4-methoxyphenyl)pyrazol-3-yloxy)-6-methoxy-7-(3-(4-methylpiperazin-1-yl)-propoxy)quinazoline,
6-methoxy-7-(2-(2-methoxyethoxy)ethoxy)-4-(5-phenylpyrazol-3-yloxy)quinazoline,
4-(5-(3-furyl)pyrazol-3-yloxy)-6-methoxy-7-(3-morpholinopropoxy)quinazoline,
6-methoxy-7-(3-morpholinopropoxy)-4-(5-phenylpyrazol-3-yloxy)quinazoline,
7-(2-(imidazol-1-yl)ethoxy)-6-methoxy-4-(5-phenylpyrazol-3-yloxy)quinazoline,
4-(5-(4-chlorophenyl)pyrazol-3-yloxy)-6-methoxy-7-(3-morpholinopropoxy)quinazoline,
6-methoxy-7-(3-(4-methylpiperazin-1-yl)propoxy)-4-(5-phenylpyrazol-3-yloxy)-quinazoline,
6-methoxy-7-(2-methoxyethoxy)-4-(5-phenylpyrazol-3-yloxy)quinazoline,
4-(5-(4-methoxyphenyl)pyrazol-3-yloxy)-6-methoxy-7-(2-(1,2,3-triazol-1-yl)ethoxy)-quinazoline and
4-(5-(4-methoxyphenyl)pyrazol-3-yloxy)-6-methoxy-7-(1-(2-methylsulphonylethyl)-piperidin-4-ylmethoxy)quinazoline,
and salts thereof.

12. (Amended) A compound as claimed in claim **18** **[4]** selected from:
7-(2-methoxyethoxy)-4-(5-phenylpyrazol-3-yloxy)quinazoline,
4-(5-(2-fluorophenyl)pyrazol-3-yloxy)-6-methoxy-7-(3-morpholinopropoxy)quinazoline,
6-methoxy-7-(3-morpholinopropoxy)-4-(5-(3-nitrophenyl)pyrazol-3-yloxy)quinazoline,
6-methoxy-7-(3-morpholinopropoxy)-4-(5-(4-nitrophenyl)pyrazol-3-yloxy)quinazoline,
6-methoxy-7-(3-morpholinopropoxy)-4-(5-(4-pyridyl)pyrazol-3-yloxy)quinazoline,
4-(5-(4-fluorophenyl)pyrazol-3-yloxy)-6-methoxy-7-(3-morpholinopropoxy)quinazoline, and
6-methoxy-7-(2-methoxyethoxy)-4-(5-(4-methoxyphenyl)pyrazol-3-yloxy)quinazoline,

and salts thereof.

13. (Amended) [The use of a compound] **The method** as claimed in claim 1 **wherein the compound is** selected from:

6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)-4-(5-phenylpyrazol-3-ylamino)-quinazoline

and

6,7-dimethoxy-4-(5-phenylpyrazol-3-yloxy)quinazoline

and pharmaceutically acceptable salts [or a salt] thereof**[, in the manufacture of a medicament for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals such as humans]**.

14. (Amended) A compound as claimed in any one of claims **[4] 18 and 5** to 12 in the form of a pharmaceutically acceptable salt.

16. (Amended) A pharmaceutical composition which comprises as active ingredient a compound of formula **II [I]** or a pharmaceutically acceptable salt thereof as claimed in any one of claims **[4] 18 and 5** to 12 in association with a pharmaceutically acceptable excipient or carrier.

17. (Amended) A method for producing an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective amount of a compound of formula **II [I]** as defined in **any one of claims 18 and 5 to 12 [claim 1]** or a pharmaceutically acceptable salt thereof.

Claim 4 has been cancelled and replaced with new claim 18.

Claim 15 has been cancelled and replaced with new claim 19.